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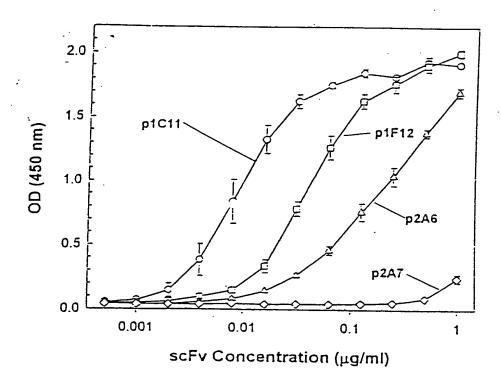


FIGURE 1

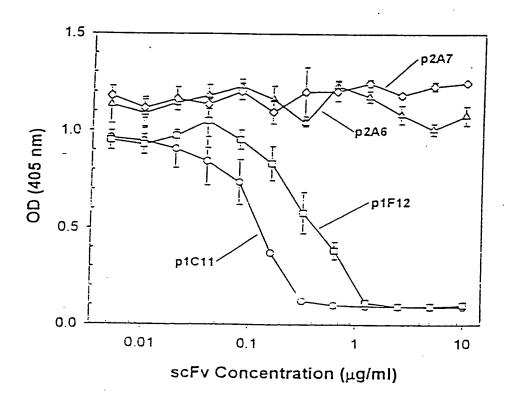


FIGURE 2

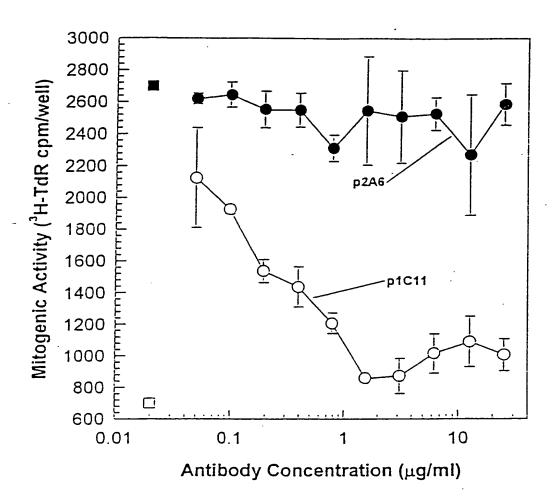


FIGURE 3

<u>GAACTT</u>ATGGGATGGTCATGTCTCATCCTTTTTCTAGTAGCAACTGCAACTGGAGTACAT MGWSCLILFLVATATGVH → leader TCAÇAGGTCAAGCTGCAGCAGTCTGGGGCAGAGCTTGTGGGGTCAGGGGCCTCAGTCAAA S Q V K L Q Q S G A E L V G S G A S V K TTGTCCTGCACAACTTCTGGCTTCAACATTAAAGACTTCTATATGCACTGGGTGAAGCAG LSCTTSGFNIKDFYMHWVKQ AGGCCTGAACAGGGCCTGGAGTGGATTGGATGGATTGATCCTGAGAATGGTGATTCTGAT RPEQGLEWIGWIDPENGDSD CDR-#2 TATGCCCCGAAGTTCCAGGGCAAGGCCACCATGACTGCAGACTCATCCTCCAACACAGCC Y A P K F Q G K A T M T A D S S S N T A TACCTGCAGCTCAGCAGCCTGACATCTGAGGACACTGCCGTCTATTACTGTAATGCATAC YLQLSSLT-SEDTAVYYCNA<u>Y</u> TATGGTGACTACGAAGGCTACTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGGTGAG Y G D Y E G Y W G Q G T T V T V S BamHI TGGATCC HindIII M G W S C I I L F L V A T A T G V H -- leader TCAGACATCGAGCTCACTCAGTCTCCAGCAATCATGTCTGCATCTCCAGGGGAGAAGGTC S D I E L T Q S P A I M S A S P G E K V ACCATAACCTGCAGTGCCAGCTCAAGTGTAAGTTACATGCACTGGTTCCAGCAGAAGCCA T I T C S A S S S V S Y M H W F Q Q K P GGCACTTCTCCCAAACTCTGGATTTATAGCACATCCAACCTGGCTTCTGGAGTCCCTGCT G T S P K L W I Y S T S.N L A S G V P A COR-L2 CGCTTCAGTGGCAGTGGATCTGGGACCTCTTACTCTCACAATCAGCCGAATGGAGGCT RFSGSGTSYSLTISRMEA GAAGATGCTGCCACTTATTACTGCCAGCAAAGGAGTAGTTACCCATTCACGTTCGGCTCG E D A A T Y Y C Q Q R S S Y P F T F G S GGGACCAAGCTGGAAATAAAACGTGAGT<u>GGATCC</u>

HindIII

FIGURE 4

GTKLEIK

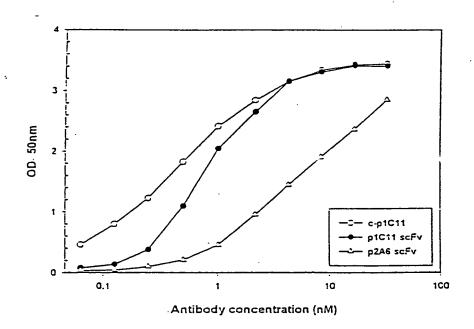


FIGURE 5

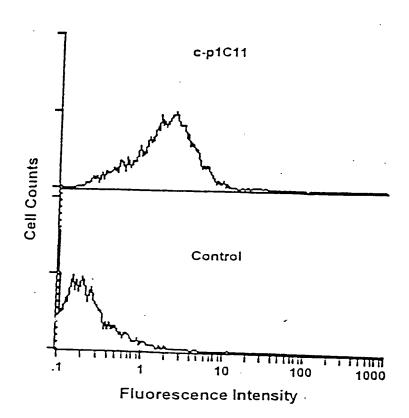


FIGURE 6

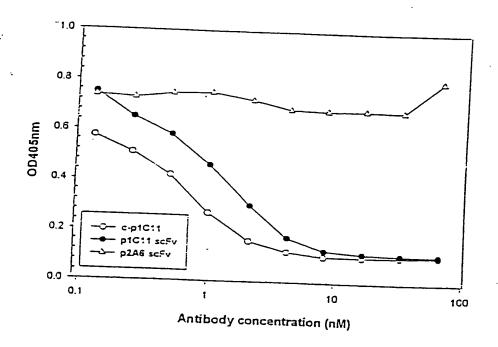


FIGURE 7

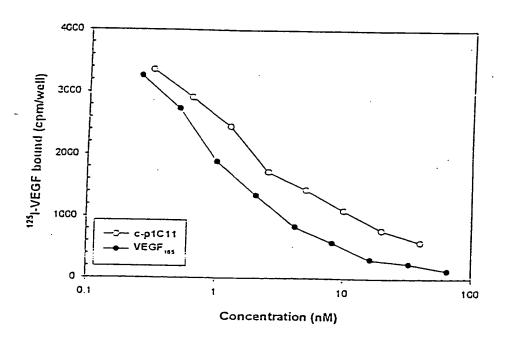


FIGURE 8

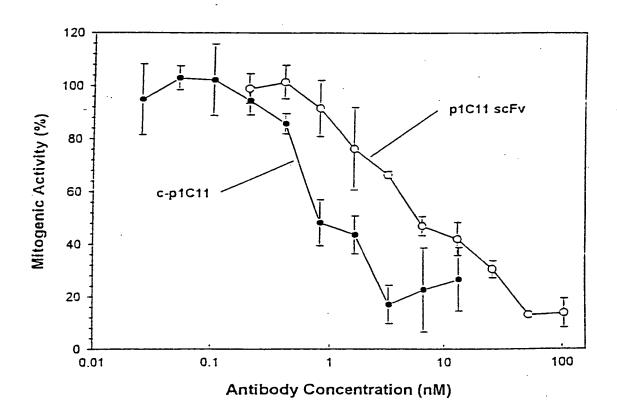


FIGURE 9

ble 1 KDR-binding analysis of anti-KDR scFv antibodies

scrv clone	KDR binding ¹ (ED50, nM)	VEGF blocking ² (IC50, nM)	Bi <i>kon</i> (10 ⁵ M ⁻¹ s ⁻¹)	Binding kinetics ³ **koff Kd** (10 ⁻¹ s ⁻¹) (10 ⁻⁹ M)	s, K <i>d</i> (10° M)	•
p1C11	yes (0.3)	yes (3.0)	_=	2.3	2.1	•
pIF12	yes (1.0)	yes (15)	0.24	1.4	5.9	
p2A6	yes (5.0)	ກວ (>300)	<u>4</u>	46.1	11.2	
p2A7	no (NA)	no (>300)	N	N	NA NA	

^{1.} Determined by direct binding ELISA, numbers in the parenthesis represent the scFv concentrations that give 50% of maximum binding (also see Fig. 4); 2. Determined by competitive VEGF blocking ELISA, numbers in the parenthesis represent the scFv concentrations required for 50% inhibition of KDR binding to immobilized VEGF (also see Fig. 2.1); 3. Determined by BIAcore , NA, not applicable.

Table 2 Binding kinetics of p1C11 scFv and c-p1C11 to KDR receptor ...

Antibody	<i>kon</i> (10 ⁵ Μ ¹ s ⁻¹)	<i>koff</i> (10 ⁻¹ s ⁻¹)	Kd (10 ⁻⁹ M)
p1C11 scFv	1.11	2.27	2.1
c-plCII	0.63	0.52	0.82
VEGF	1.87	1.81	0.93

^{*} All rates are determined by surface plasmon resonance using BIAcore system ..., and are mean of at least three separate determinations.